

### REMARKS

Claims 40, 41, 45, 54, 57, 59, 62, 63, 68, 70, 78, 80, 81, 88, 123, 126-128, and 140-180 are pending in the present application. New claims 141-180 are supported in the specification, for example, at Figures 2, 4, and 5, SEQ ID NOs: 3, 4, 5, and 6, at page 6, line 38 to page 7, line 12, page 14, lines 21-36, page 15, lines 15-17, page 16, lines 19-29, and page 38, line 32 to page 41, line 17, and by the Italian priority document FI92A 000052 (see below). Claims 45, 54, 57, 59, 62, 63, 70, 78, 80, 81, 123, 126, and 140 are amended. Claims 1-39, 42-44, 46-53, 55, 56, 58, 60, 61, 64-67, 69, 71-77, 79, 82-87, 89-122, 124, 125, and 129-139 are canceled. No new matter has been introduced by this amendment.

Preliminarily, Applicants note with appreciation the indication of allowability of claims 40, 41, and 127 and of rejections mooted or withdrawn as listed at pages 3-4 of the present Office Action.

**No new matter has been introduced into the specification.**

An objection to the language "the entire contents of each application is incorporated by reference herein" set forth in the amendment filed July 25, 2002 has been raised in the Office Action for alleged introduction of new matter into the specification. Applicants respectfully disagree. A preliminary amendment accompanied the present application upon its filing on July 26, 1999. That preliminary amendment contained the language to which the Patent Office now objects. As the preliminary amendment containing the incorporation by reference was included with the specification upon its filing, the incorporation by reference included in the amendment filed July 25, 2002 does not contain new matter. Withdrawal of the objection is respectfully requested.

**Amended claims 45, 54, 62, 68, 78, 81, and 88 do not contain new matter.**

Claims 45, 47, 54, 56, 62, 68, 78, 81, and 88 allegedly contain new matter in recitation of a polypeptide having at least five, ten, or fifteen contiguous amino acids of amino acids 750-977 of the amino acid sequence of SEQ ID NO:5. Applicants have amended claims 45, 54, 62, 78, and 81 to recite a polypeptide comprising amino acids 750-977 of the amino acid sequence of SEQ ID NO:5 and have canceled claims 47 and 56. The Italian

priority document FI92A 000052, the priority benefit of which has been properly claimed, discloses a protein sequence deduced from a *Helicobacter pylori*-derived polynucleotide comprising the amino acid sequence set forth in Figure 3C of that document. One of ordinary skill in the art would understand that the sequence disclosed in the priority document corresponds to amino acids 750-977 of the amino acid sequence of the cytotoxin associated antigen (SEQ ID NO:5) of the present specification in view of the description of the CagA protein set forth in the priority document (for example, a protein extracted from cytotoxic strains of *Helicobacter pylori* having a molecular weight of about 130 kDa comprising the amino acid sequence set forth in claim 2 and Figure 3C of that document) and the description of the same protein in the present application (see the present specification, for example, at page 6, lines 12-39 and at pages 47-55). Applicants respectfully note that reference to the amino acids of Figure 3C and claim 2 of the priority document as amino acids 750-977 of the amino acid sequence of SEQ ID NO:5 of the present application is in accordance with MPEP 2422.03. Applicants respectfully submit that no new matter is present in the amended claims. Withdrawal of the rejection is respectfully requested.

**Amended claim 123 contains no new matter.**

Claims 123-125 are rejected under 35 U.S.C. § 112, first paragraph for allegedly containing new matter in recitation of a polypeptide encoded by at least fifteen, thirty, or forty-five nucleotides of nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO:4. Applicants have amended claim 123 to recite an isolated immunogenic polypeptide encoded by a polynucleotide sequence comprising nucleotides 2782-3466 of the nucleotide sequence of SEQ ID NO:4 and have canceled claims 124 and 125. The Italian priority document FI92A 000052 discloses a nucleotide sequence derived from *Helicobacter pylori* as set forth in Figure 3B and claim 3 of that document. One of ordinary skill in the art would understand that the sequence disclosed in the priority document corresponds to nucleotides 2782-3466 of the nucleotide sequence encoding the cytotoxin associated antigen (SEQ ID NO:4) of the present specification in view of the description of the CagA protein and its nucleotide sequence set forth in the priority document (for example, a protein extracted from cytotoxic strains of *Helicobacter pylori* having a molecular weight of about 130 kDa comprising the amino acid sequence set forth in claim 2 and Figure 3C of that document and encoded by the

nucleotide sequence of claim 3 and Figure 3B) and the description of the same protein and its encoding nucleic acid sequence in the present application (see the present specification, for example, at page 6, lines 12-39 and at pages 47-55). Applicants respectfully note that reference to the nucleotides of Figure 3B and claim 3 of the priority document as nucleotides 2782-3466 of the sequence of SEQ ID NO:4 of the present application is in accordance with MPEP 2422.03. Applicants respectfully submit that no new matter is present in amended claim 123. Withdrawal of the rejection is respectfully requested.

**Claims 57, 59, 63, 70, 80, 126, 128, and 140 as amended satisfy 35 U.S.C. § 112.**

Claims 57, 59, 63, 70, 80, 126, 128, and 140 are rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness.

Claim 57 is allegedly indefinite in recitation of the phrase “at least ten contiguous amino acids of the amino acid sequence of SEQ ID NO:5, wherein said polypeptide includes *at least one of* the amino acid sequences selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and six contiguous asparagines residues.” Applicants have amended the claim to recite the term “comprising.” As the term comprising is open-ended, it would be clear to one of ordinary skill in the art that a polypeptide comprising at least ten contiguous amino acids may have more than ten amino acids, for example, SEQ ID NO:9. Withdrawal of the rejection is respectfully requested.

Applicants have amended claims 57, 59, 63, and 140 to clarify that the heat shock protein comprises the amino acid sequence of SEQ ID NO:6. Applicants have similarly amended claims 70 and 80 to clarify that the cytotoxin comprises the amino acid sequence of SEQ ID NO:3. Claim 126 has been amended to clarify that the recited polypeptide comprises a *Helicobacter pylori* cytotoxin associated immunodominant antigen having the amino acid sequence of SEQ ID NO:5 encoded by at least fifteen contiguous nucleotides of the nucleotide sequence of SEQ ID NO:4. Withdrawal of the rejections is respectfully requested.

Applicants have amended claim 57 to insert a space between the words “and” and “an.” Withdrawal of the rejection is respectfully requested.

Withdrawal of the rejection of claims 59 and 128 is respectfully requested in view of the amendments to claims 57 and 126.

**Amended claims 81 and 88 are patentable over the Peterson reference.**

Claims 81 and 88 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by Peterson *et al.* (*Nature*, 354:369-373 (1991)) (“the Peterson reference”). Applicants have amended claim 81 to recite isolated immunogenic polypeptides comprising a *Helicobacter pylori* cytotoxin associated immunodominant antigen (CAI) comprising amino acids 750-977 of the amino acid sequence of SEQ ID NO:5. Withdrawal of the rejection of claims 81 and 88 is respectfully requested.

**Amended claims 81 and 88 are patentable over the Guntaka reference.**

Claims 81 and 88 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by Guntaka *et al.* (*Biochem. Biophys. Res. Commun.*, 182:412-419 (1991)) (“the Guntaka reference”). Applicants have amended claim 81 to recite isolated immunogenic polypeptides comprising a *Helicobacter pylori* cytotoxin associated immunodominant antigen (CAI) comprising amino acids 750-977 of the amino acid sequence of SEQ ID NO:5. Withdrawal of the rejection of claims 81 and 88 is respectfully requested.

**Amended claims 123, 126, and 128 are patentable over the Cover I patent.**

Claims 123-126 and 128 are rejected under 35 U.S.C. § 102(e)(2) for alleged anticipation by U.S. Patent No. 5,403,924 to Cover *et al.* (“the Cover I patent”). Claims 124 and 125 have been canceled.

Applicants respectfully assert that the present invention as defined by amended claims 123, 126, and 128 is entitled to priority over the Cover patent. Applicants’ disclosure of amino acids 750-977 of SEQ ID NO:5 and nucleotides 2782-3466 of SEQ ID NO:4 in Figures 3B and 3C and claims 2 and 3 of the Italian priority document (FI92A/000052) is entitled to a priority date of March 2, 1992. The Cover patent was filed October 13, 1992. Accordingly, the Cover patent should not qualify as prior art as to the claimed subject matter. Withdrawal of the rejection is respectfully requested.

**Amended claims 45, 54, 62, 68, 78, 81, 88, 123, and 128 are patentable over the Covacci reference.**

Claims 45, 47, 54, 56, 62, 68, 78, 81, 88, 123-125, and 128 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by Covacci *et al.* (*PNAS*, 90:5791-5795 (1993)). Claims 47 and 56 have been canceled. Applicants respectfully assert that the present invention as defined by amended claims 45, 54, 62, 68, 78, 81, 88, 123, and 128 is entitled to priority over the Covacci reference. Applicants respectfully assert that their disclosure of amino acids 750-977 of SEQ ID NO:5 and nucleotides 2782-3466 of SEQ ID NO:4 in Figures 3B and 3C and claims 2 and 3 of the Italian priority document (FI92A/000052) is entitled to a priority date of March 2, 1992. Accordingly, the Cover patent should not qualify as prior art as to the claimed subject matter. Withdrawal of the rejection is respectfully requested.

**Amended claims 57, 59, 70, and 80 are patentable over the Figura patent.**

Claims 57, 59, 70, and 80 are rejected for alleged anticipation by U.S. Patent No. 5,900,372 to Figura *et al.* ("the Figura patent") as evidenced by U.S. Patent No. 5,866,375 to Figura *et al.* Claims 57 and 70 have been amended to recite purified polypeptides. Withdrawal of the rejection is respectfully requested.

**Amended claim 63 is patentable over the Cover I patent in view of the Dunn or Evans and Hirschl references.**

Claim 63 is rejected under 35 U.S.C. § 103 for alleged obviousness over the Cover I patent and Dunn *et al.* (*Infect. Immun.*, 60:1946-1951 (1992)) ("the Dunn reference") or Evans *et al.* (*Infect. Immun.*, 60:2125-2127 (1992)) ("the Evans reference") in view of a reference by Hirschl *et al.* cited as (*Eur. J. Clin. Microbiol. Infect. Dis.*, 7:100-105 (1988)) ("the Hirschl reference"). In view of the reference on page 11 of the Office Action to pages 143-144 and Table 3 of the Hirschl reference, Applicants respectfully submit that the citation to the Hirschl reference provided by the Office Action is incorrect. Applicants respectfully submit that the correct citation for the Hirschl reference is Hirschl *et al.* in *HELICOBACTER PYLORI, GASTRITIS AND PEPTIC ULCER*, eds. Malfertheiner and Ditschuneit, Springer-Verlag, Berlin Heidelberg (1990) and have treated the rejection as such in an effort to be fully

responsive. Appropriate correction of the citation on the record is respectfully requested. Applicants have amended claim 63 to clarify that the first and second polypeptides are purified. The Hirschl reference does not teach or suggest a method of preparing an immunogenic composition comprising two purified polypeptides. Withdrawal of the rejection is respectfully requested.

**Amended claim 140 is patentable over the Cover I and II patents in view of the Hirschl reference.**

Claim 140 is rejected under 35 U.S.C. § 103 for alleged obviousness over the Cover I patent and U.S. Patent No. 6,054,132 to Cover *et al.* ("the Cover II patent") in view of the Hirschl reference. In view of the reference on page 13 of the Office Action to pages 143-144 and Table 3 of the Hirschl reference, Applicants respectfully submit that the citation to the reference provided by the Office Action is incorrect. Applicants respectfully submit that the correct citation for the Hirschl reference is Hirschl *et al.* in *HELICOBACTER PYLORI, GASTRITIS AND PEPTIC ULCER*, eds. Malfertheiner and Ditschuneit, Springer-Verlag, Berlin Heidelberg (1990) and have treated the rejection as such in an effort to be fully responsive. Appropriate correction of the citation on the record is respectfully requested. Applicants have amended claim 140 to depend from claim 63 and to clarify that the first and second polypeptides are purified. The Hirschl reference neither teaches nor suggests a method of preparing an immunogenic composition comprising two purified polypeptides. Withdrawal of the rejection is respectfully requested.

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**PATENT**

### **CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, the undersigned may be contacted at 215-557-5908.

Respectfully submitted,



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